

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
30 June 2005 (30.06.2005)

PCT

(10) International Publication Number
WO 2005/058175 A1

(51) International Patent Classification⁷: **A61B 17/86**
(21) International Application Number:
PCT/GB2004/005280

(74) Agent: **BELCHER, Simon, James; Urquhart-Dykes & Lord LLP**, Tower North Central, Merrion Way, Leeds LS2 8PA (GB).

(22) International Filing Date:
16 December 2004 (16.12.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
0329596.1 19 December 2003 (19.12.2003) GB
0406825.0 25 March 2004 (25.03.2004) GB

(71) Applicant (for all designated States except US): **DEPUY INTERNATIONAL LIMITED** [GB/GB]; St. Anthony's Road, Beeston, Leeds LS11 8DT (GB).

(72) Inventors; and

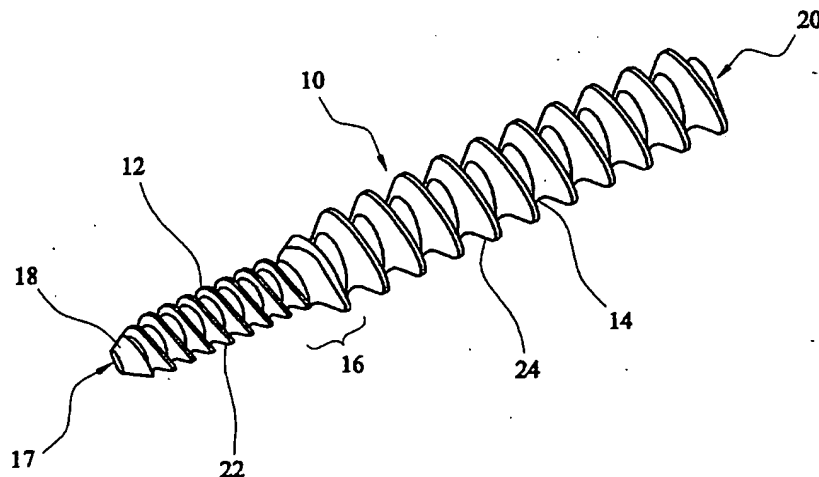
(75) Inventors/Applicants (for US only): **HES, Robert** [—/BE]; Molenbeemd 16, B-2970 Schilde (BE). **CONIX, Bart** [—/BE]; Kleine Wandelweg 16, B-2980 Zoersel (BE). **GOWLAND, Christopher** [GB/GB]; 43 Swanhill Lane, Pontefract, West Yorkshire WF8 2QN (GB).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

[Continued on next page]

(54) Title: **A BONE SCREW**



(57) Abstract: A bone screw (10) having a lead portion (12) and a tail portion (14), each comprising a root and a thread (22, 24) (having a thread lead) formed on the root. The thread on each of the lead and tail portions has an approximately constant diameter along a significant portion of its length. The diameter of the thread on the tail portion is greater than that of the thread on the lead portion, and in which the thread lead of the thread on the lead portion is equal to the thread lead of the thread on the tail portion. The screw can be used to achieve fixation to a vertebra with an anterior approach.

WO 2005/058175 A1



Published:

— with international search report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

-1-

A BONE SCREW

This invention relates to a bone screw. The bone screw can be used for example for screw fixation to a vertebra.

Bone screws can be used to fasten components to bone tissue. For example, bone screws can be used to fasten implant components to a bone. Examples of implant components include fracture plates which can be fastened across a fracture to hold fractured parts of a bone in alignment during healing. Bone screws can be used to fasten instruments to bone during surgery. Examples of instruments which might require such fastening include alignment rods and resection blocks.

A bone screw can be used to fasten a component to a vertebra, for example in the treatment of a defect in a patient's spine such as a fracture within a vertebra, or a defective (for example degenerative) inter-vertebral body (disc). For example, a bone screw can be used to fasten anchor blocks to a vertebra. A bar or plate can be connected to the spine at a number of vertebrae using such anchor blocks, to immobilise (for example by fusing) a segment of the spine.

Screws used for fixation to a vertebra are commonly referred to pedicle screws. An example of a pedicle screw is disclosed in WO-90/02526. Pedicle screws are conventionally inserted using a posterior approach, in which the screw extends through the pedicle into the vertebral body.

Bone in the vertebral body comprises cancellous bone tissue, characterised by voids and a low density. Bone in the pedicles comprises cortical bone tissue, which has a higher density than cancellous bone tissue. Cortical bone tissue is stronger than cancellous bone tissue and is better able to provide a secure connection for screw fixation. However, the width of the bone screw is restricted by the narrow transverse dimension of the pedicle. It can therefore mean that the contribution of the cancellous bone tissue to the screw fixation is significantly compromised because the structure of the cancellous bone requires that the thread has a large diameter in order for the fixation to it to be secure.

-2-

The present invention provides a bone screw which can be used for fixation to a bone whose structure or dimensions differ from one region to another, which has lead and tail portions, each having an approximately constant diameter over a significant portion of its length, in which the diameter of the thread on the tail portion is greater than that of the thread on the lead portion, and in which the thread lead of the thread on the lead portion is equal to the thread lead of the thread on the tail portion.

Accordingly, in one aspect, the invention provides a bone screw having a lead portion and a tail portion, each comprising a root and a thread (having a thread lead) formed on the root, the thread on each of the lead and tail portions having an approximately constant diameter along a significant portion of its length, in which the diameter of the thread on the tail portion is greater than that of the thread on the lead portion, and in which the thread lead of the thread on the lead portion is equal to the thread lead of the thread on the tail portion.

The bone screw of the invention has the advantage that it can be used to form a secure fixation to a bone which has regions with different characteristics such as dimensions, bone density, in which the lead portion of the screw is received in a first region of the bone and the tail portion of the screw is received in a second region. For example, the bone in the first region might comprise cortical tissue and the bone in the second region might comprise cancellous tissue. The transverse dimension of the bone in the first region might be smaller than that in the second region.

The bone screw of the invention finds particular application in screw fixation to a vertebra, in which the screw is inserted into the vertebra anteriorly, via the vertebral body into a pedicle.

The lead and tail portions of the bone screw should be connected to one another so that it is not possible for one of them to be rotated relative to the other, preferably in both rotational directions. This can be achieved by forming the bone screw as a single body, for example by a moulding (casting) process, or by machining the screw from a single block (especially a single block of a metal). If the lead and tail portions of the screw are formed as separate

-3-

parts, they should generally be capable of being fastened to one another so that they are incapable of relative rotation in at least one, preferably each direction. This allows the bone screw to be driven into a bone by the application of rotational forces from the tail end.

In another aspect, the invention provides a method of screw fixation to a vertebra, which comprises exposing an anterior surface of the vertebra to receive a screw, and inserting a bone screw into the vertebra, via the vertebral body into a pedicle. The screw that is used in the method can be a bone screw according to the invention.

Significant advantages arise from insertion of a bone screw into a vertebra using an anterior approach. Exposure of bone tissue anteriorly involves less resection of muscle and other tissue compared with a posterior approach. This can give rise to advantages of reduced blood loss, reduced patient trauma, and reduced recovery time.

Furthermore, insertion of a bone screw into a pedicle through the cancellous tissue of the vertebral body allows the screw to be constructed with threads whose features are optimised for fixation to the bone tissues in the two regions of the bone. In particular, the diameter of the tail portion of the screw can be greater than the diameter of the lead portion: a large diameter in the tail portion can enhance the security of the fixation in the cancellous tissue.

Preferably, the thread on the lead portion of the screw is a multi-start thread. This has the advantage of providing a thread on the lead portion which has a smaller pitch than would be the case if the thread is a single-start thread. This can enhance the security of the fixation in cortical bone tissue.

Preferably, the number of starts of the thread on the lead portion is equal to the ratio of the thread pitch of the thread on the tail portion to the thread pitch of the thread on the lead portion. For example, the thread on the lead portion of the screw can be a double-start thread with the thread on the tail portion of the screw being a single-start thread; preferably, the thread pitch of the thread on the tail portion is then equal to twice the thread pitch of the thread on the lead portion.

-4-

The thread pitch is the distance along the axis of the screw between adjacent thread peaks. The thread lead is the distance that is travelled along the axis of the screw in one complete 360° revolution of the screw. When the thread on the lead portion of the screw is a multi-start thread, it is preferred that the number of starts of the thread is equal to the ratio of the thread lead to the thread pitch.

Preferably, the ratio of the diameter of the thread on the tail portion to that of the diameter of the thread on the lead portion is at least about 1.2, more preferably at least about 1.5. When the bone screw is intended for use in a vertebra, the relative sizes of the lead and tail portions of the screw can be selected to ensure that the diameter of the lead portion is not greater than the transverse dimension of the pedicle, while also providing sufficiently large diameter in the tail portion to provide secure fixation in the cancellous tissue. Preferably, the ratio of the diameter of the thread on the tail portion to the diameter of the thread on the lead portion is not more than about 2.3, preferably not more than about 2.0.

Generally, the diameter of the root of the tail portion is greater than the diameter of the root of the lead portion. The ranges for the ratio of the diameter of the thread on the tail portion to the diameter of the thread on the lead portion can also apply to the ratio of the diameter of the root of the tail portion to the diameter of the root of the lead portion.

Preferably, the diameter of the lead portion of the bone screw is at least about 3 mm, more preferably at least about 4.5 mm, for example at least about 6 mm. Preferably, the diameter of the lead portion of the screw is not more than about 15 mm, more preferably not more than about 13 mm, for example not more than about 11 mm.

Preferably the diameter of the root of the lead portion is at least about 2.5 mm, more preferably at least about 3.5 mm, for example at least about 4 mm. Preferably, the diameter of the root of the lead portion is not more than about 7 mm, more preferably not more than about 6 mm, for example not more than about 5 mm.

Preferably the diameter of the root of the tail portion is at least about 3 mm, more preferably at least about 4 mm, for example at least about 5 mm. Preferably, the diameter of the

-5-

root of the tail portion is not more than about 10 mm, more preferably not more than about 8 mm, for example not more than about 7 mm.

Preferably, the ratio of the diameter of the root of the tail portion to the diameter of the root of the lead portion is at least about 1.2, more preferably at least about 1.4. Preferably, the ratio of the diameter of the root of the tail portion to the diameter of the root of the lead portion is not more than about 2.3, more preferably not more than about 2.0.

Preferably, the value of the thread aspect ratio, defined by the expression:

$$\text{Thread aspect ratio} = \frac{(\text{Overall diameter}) - (\text{Root diameter})}{2 \times (\text{Root diameter})}$$

in respect of the thread on the tail portion is greater than that in respect of the thread on the lead portion. It has been found that a higher thread aspect ratio for the thread on the tail portion can help to make a secure screw fixation to cancellous bone. For example, the ratio of the thread aspect ratio of the thread on the tail portion to the thread aspect ratio of the thread on the lead portion might be at least about 1.2, preferably at least about 1.35.

Preferably, the ratio of the thread aspect ratio of the thread on the tail portion to the thread aspect ratio of the thread on the lead portion is not more than about 2.2, more preferably not more than about 2.0.

For example, the thread aspect ratio in the lead portion might be at least about 0.15, preferably at least about 0.2. The thread aspect ratio in the lead portion might be not more than about 0.4, preferably not more than about 0.3, especially not more than 0.25. The thread portion of the tail portion might be at least about 0.25, preferably at least about 0.3. The thread aspect ratio in the tail portion might be not more than about 0.5, preferably not more than about 0.4, especially not more than 0.35.

Preferably, the bone screw has a bore extending through it along its length. This can facilitate use of a guidewire to locate and to orientate the bone screw. The bone screw of

-6-

the invention can be supplied as a part of a kit, which also includes a guidewire which is a close fit in the bore in the bone screw.

Materials for the bone screw should be inert towards body fluid with which the screw will come into contact when it is in use. It should also be capable of withstanding the stresses to which it will be subjected during fixation and once fixed to the bone. Suitable materials include certain stainless steel alloys, and titanium and certain titanium based alloys. Materials which can be used in the manufacture of bone screws are known.

Preferably, the thread at the end of the lead portion of the screw is self-starting. For example, the diameter of the thread towards the end of the lead portion can be reduced towards the end of the screw, relative to the diameter of the thread on the lead portion where it is approximately constant.

Preferably, the screw has a transition portion between the lead and tail portions. For example, the diameter of the screw can increase gradually between the lead and tail portions over the transition portion. The bone screw can comprise a root with a thread formed on it in the transition portion; preferably, the thread in the transition portion is a continuation of the thread on the tail portion, in which the diameter of the thread in the transition portion is reduced towards the lead portion.

Preferably, the thread on the tail portion of the screw is a continuation of the thread on the lead portion. When the thread on the lead portion of the screw is a multi-start thread, the thread on the tail portion of the screw is preferably a continuation of one of the threads on the lead portion.

The bone screw will generally be provided with formations at its tail end for engaging a tool by which torque can be applied to the screw to drive it into the bone. Suitable formations include recesses shaped as, for example, slots, crosses, stars, polygons (especially hexagons), and multiple lobes (especially hexlobes).

-7-

Embodiments of the invention will now be described by way of example with reference to the accompanying drawings, in which:

Figure 1 is a schematic side view of a portion of a spine, having a vertebra in which a bone screw according to the invention has been implanted.

Figure 2 is a side view of a bone screw of the kind which is shown in Figure 1 implanted in a vertebra.

Figures 3 and 4 are enlarged side views showing details of the threads on the bone screw shown in Figure 2, in the lead and tail portions.

Referring to the drawings, Figure 1 shows a portion of a spine which comprises a plurality of vertebrae 2 separated by disks 4. Each of the vertebrae 2 comprises a vertebral body 6 and two posteriorly directed pedicles (of which one 8 is visible on each of the vertebrae).

Conventionally, a bone screw is inserted into a vertebra using a posterior approach so that the screw passes through the cortical bone of a pedicle into the cancellous bone of the vertebral body.

According to the invention, a bone screw 10 is implanted into a vertebra using an anterior approach, so that the screw passes through the cancellous bone of the vertebral body 6 into the cortical bone of the pedicle 8.

Figure 2 shows a bone screw 10 which is configured for implantation into a vertebra using an anterior approach. The screw has a lead portion 12 and a tail portion 14, and an intermediate transition portion 16. Each of them comprises a root which has a helical thread formed on it. The screw has a bore 17 extending through it.

The thread on each of the lead and tail portions has a constant diameter over almost the entire length of the respective portion. The tip 18 of the bone screw is tapered towards a

-8-

point. The opposite end of the bone screw has a hexagonal socket 20 formed in it which can receive the end of a hexagonal driver tool.

The thread 22 on the lead portion is a double-start thread, in which two threads are arranged around the root, equally spaced around the axis of the screw. The thread is optimised in terms of the aspect ratio for fixation in cortical bone tissue. Because the thread on the lead portion is a double-start thread, the thread pitch on the lead portion is equal to half the thread lead. Details of the thread 22 are shown in Figure 3.

The thread 24 on the tail portion is a single-start thread, in which the thread pitch and the thread lead are equal to the thread lead on the lead portion. The thread is optimised in terms of the aspect ratio for fixation in cancellous bone tissue. The thread on the tail portion is continuous with one of the threads on the lead portion, through the transition portion of the screw in which the root and the thread taper. Details of the thread 24 are shown in Figure 4.

Dimensions (in millimetres) of a preferred embodiment of screw, which can be suitable for use as a pedicle screw, are as follows:

| | | |
|--------------|---------------------|------|
| Overall | Length | 70.0 |
| | Bore diameter | 2.0 |
| Lead portion | Length | 20.0 |
| | Thread pitch | 2.25 |
| | Thread lead | 4.5 |
| | Root diameter | 4.5 |
| | Overall diameter | 6.5 |
| | Thread aspect ratio | 0.22 |
| | | |
| Tail portion | Length | 46.0 |
| | Thread pitch | 4.5 |
| | Thread lead | 4.5 |
| | Root diameter | 6.5 |
| | Overall diameter | 10.5 |
| | Thread aspect ratio | 0.31 |

-9-

CLAIMS:

1. A bone screw having a lead portion and a tail portion, each comprising a root and a thread (having a thread lead) formed on the root, the thread on each of the lead and tail portions having an approximately constant diameter along a significant portion of its length, in which the diameter of the thread on the tail portion is greater than that of the thread on the lead portion, and in which the thread lead of the thread on the lead portion is equal to the thread lead of the thread on the tail portion.
2. A bone screw as claimed in claim 1, in which the thread on the lead portion of the screw is a multi-start thread.
3. A bone screw as claimed in claim 2, in which the number of starts of the thread on the lead portion is equal to the ratio of the thread pitch of the thread on the tail portion to the thread pitch of the thread on the lead portion.
4. A bone screw as claimed in claim 2, in which the thread on the lead portion of the screw is a double-start thread and the thread on the tail portion of the screw is a single-start thread, and in which the thread pitch of the thread on the tail portion is equal to twice the thread pitch of the thread on the lead portion.
5. A bone screw as claimed in claim 2, in which the thread on the tail portion of the screw is a continuation of one of the threads on the lead portion.
6. A bone screw as claimed in claim 1, in which the ratio of the diameter of the thread on the tail portion to that of the diameter of the thread on the lead portion is at least about 1.2, preferably at least about 1.5.
7. A bone screw as claimed in claim 1, in which the ratio of the diameter of the thread on the tail portion to the diameter of the thread on the lead portion is not more than about 2.3, preferably not more than about 2.0.

-10-

8. A bone screw as claimed in claim 1, in which the diameter of the root of the tail portion is greater than the diameter of the root of the lead portion.
9. A bone screw as claimed in claim 8, in which the ratio of the diameter of the root of the tail portion to the diameter of the root of the lead portion is at least about 1.2, preferably at least about 1.4.
10. A bone screw as claimed in claim 8, in which the ratio of the diameter of the root of the tail portion to the diameter of the root of the lead portion is not more than about 2.3, preferably not more than about 2.0.
11. A bone screw as claimed in claim 1, in which the value of the thread aspect ratio, defined by the expression:

$$\text{Thread aspect ratio} = \frac{(\text{Overall diameter}) - (\text{Root diameter})}{2 \times (\text{Root diameter})}$$

in respect of the thread on the tail portion is greater than that in respect of the thread on the lead portion.

12. A bone screw as claimed in claim 11, in which the ratio of the thread aspect ratio of the thread on the tail portion to the thread aspect ratio of the thread on the lead portion is at least about 1.2, preferably at least about 1.35.
13. A bone screw as claimed in claim 11, in which the ratio of the thread aspect ratio of the thread on the tail portion to the thread aspect ratio of the thread on the lead portion is not more than about 2.2, preferably not more than about 2.0.
14. A bone screw as claimed in claim 1, which has a bore extending through it along its length.

-11-

15. A method of screw fixation to a vertebra, which comprises exposing an anterior surface of the vertebra to receive a screw, and inserting a bone screw into the vertebra, via the vertebral body into a pedicle.

16. A method as claimed in claim 15, in which the screw is as claimed in any one of claims 1 to 14.

-1/2-

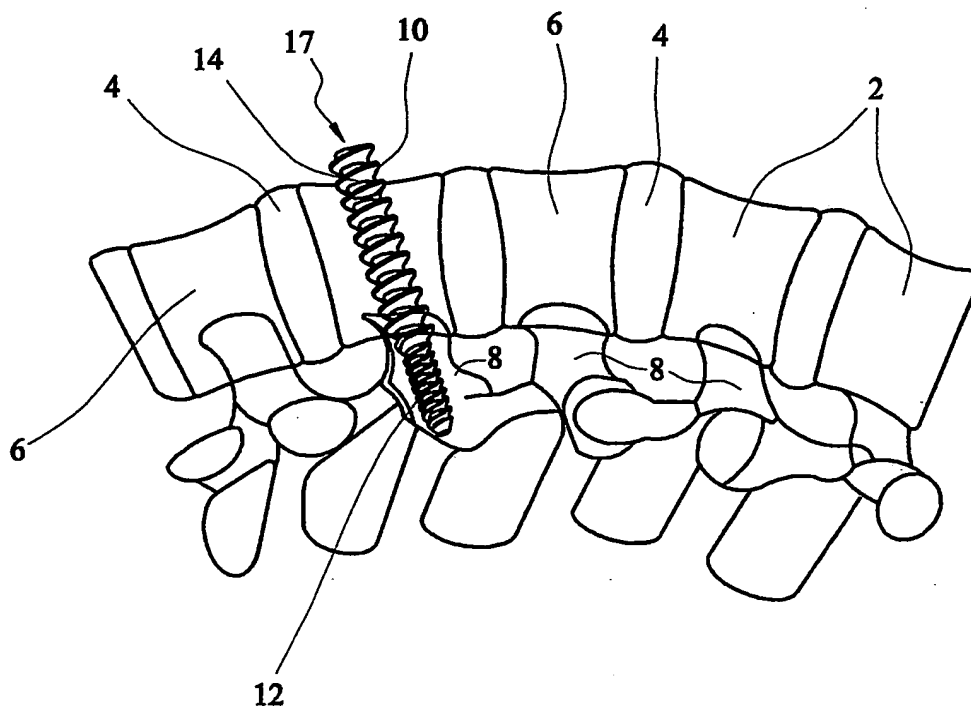


FIG. 1

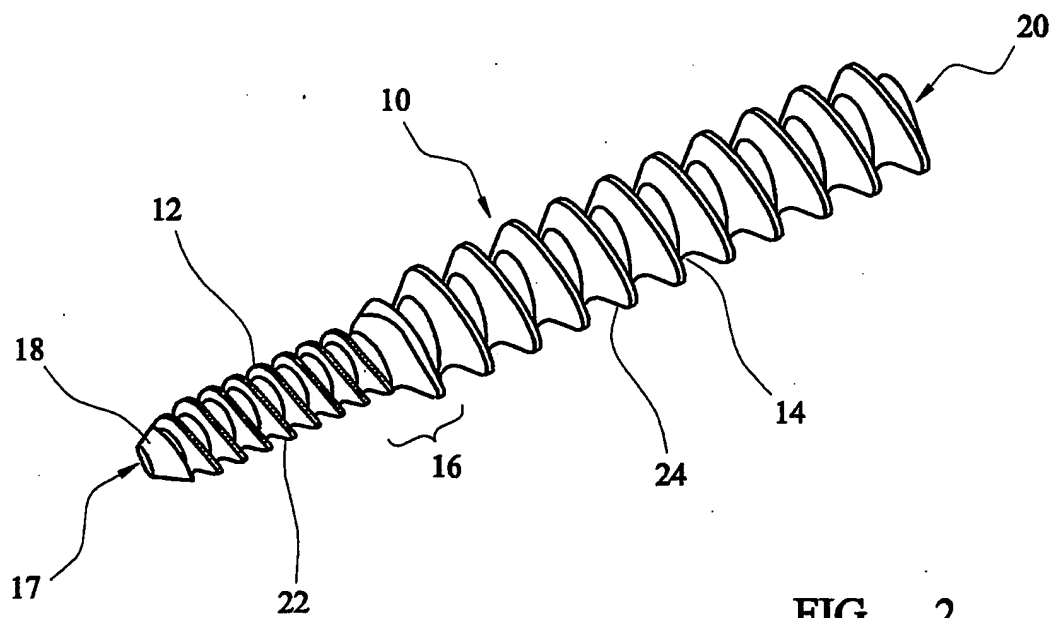


FIG. 2

-2/2-

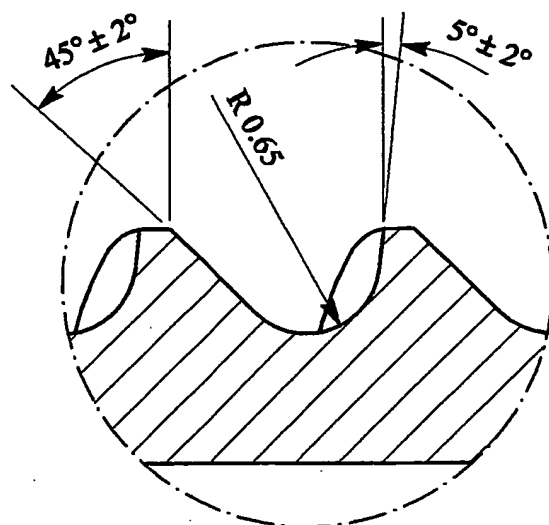


FIG. 3

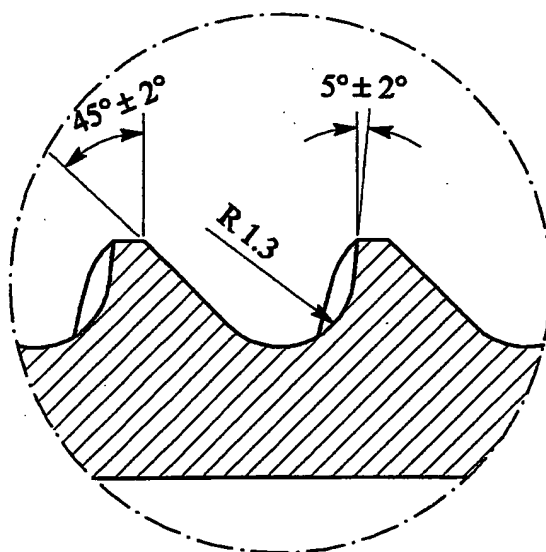


FIG. 4

INTERNATIONAL SEARCH REPORT

PCT/GB2004/005280

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61B17/86

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|--------------------------------------------------------------------------------------------------|-----------------------|
| X | US 5 593 410 A (VRESPA ET AL) 14 January 1997 (1997-01-14) | 1-4,6-10 |
| Y | figures 1,8 | 5,14 |
| X | US 5 180 382 A (FRIGG ET AL) 19 January 1993 (1993-01-19) | 1,6-13 |
| Y | figure 1 | 14 |
| X | US 6 355 043 B1 (ADAM MICHAEL) 12 March 2002 (2002-03-12) | 1,6,7, 11-13 |
| Y | | 14 |
| Y | US 6 129 730 A (BONO ET AL) 10 October 2000 (2000-10-10) column 4, paragraph 4 figure 4 | 5 |
| | -/- | |

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
- *G* document member of the same patent family

Date of the actual completion of the international search

5 April 2005

Date of mailing of the international search report

12/04/2005

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax (+31-70) 340-3016

Authorized officer

Schießl, W

INTERNATIONAL SEARCH REPORT

PCT/GB2004/005280

| C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT | | |
|------------------------------------------------------|------------------------------------------------------------------------------------------|-----------------------|
| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
| Y | EP 1 273 273 A (DEPUY FRANCE; BAROUK, LOUIS SAMUEL) 8 January 2003 (2003-01-08) figure 2 | 14 |

INTERNATIONAL SEARCH REPORT

PCT/GB2004/005280

Box II Observations where certain claims were found unsearchable (Continuation of Item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 15, 16
because they relate to subject matter not required to be searched by this Authority, namely:
Rule 39.1(iv) PCT - Method for treatment of the human or animal body by surgery
Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of Item 3 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

PCT/GB2004/005280

| Patent document cited in search report | | Publication date | | Patent family member(s) | Publication date |
|-------------------------------------------|----|---------------------|----|----------------------------|---------------------|
| US 5593410 | A | 14-01-1997 | IT | 1237496 B | 08-06-1993 |
| | | | AT | 119011 T | 15-03-1995 |
| | | | AT | 146061 T | 15-12-1996 |
| | | | CA | 2028597 A1 | 27-04-1991 |
| | | | DE | 69017349 D1 | 06-04-1995 |
| | | | DE | 69017349 T2 | 29-06-1995 |
| | | | DE | 69029404 D1 | 23-01-1997 |
| | | | DE | 69029404 T2 | 07-05-1997 |
| | | | DK | 424734 T3 | 22-05-1995 |
| | | | EP | 0424734 A1 | 02-05-1991 |
| | | | EP | 0557899 A1 | 01-09-1993 |
| | | | EP | 0554915 A1 | 11-08-1993 |
| | | | ES | 2070236 T3 | 01-06-1995 |
| | | | US | 5259398 A | 09-11-1993 |
| US 5180382 | A | 19-01-1993 | DE | 9017101 U1 | 11-04-1991 |
| | | | CA | 2057957 A1 | 20-06-1992 |
| | | | EP | 0491211 A1 | 24-06-1992 |
| | | | JP | 2538470 B2 | 25-09-1996 |
| | | | JP | 4295348 A | 20-10-1992 |
| US 6355043 | B1 | 12-03-2002 | AT | 265825 T | 15-05-2004 |
| | | | DE | 50006293 D1 | 09-06-2004 |
| | | | EP | 1033111 A1 | 06-09-2000 |
| | | | ES | 2220379 T3 | 16-12-2004 |
| US 6129730 | A | 10-10-2000 | AU | 3486100 A | 29-08-2000 |
| | | | WO | 0047120 A1 | 17-08-2000 |
| EP 1273273 | A | 08-01-2003 | AU | 5072202 A | 09-01-2003 |
| | | | CA | 2390912 A1 | 05-01-2003 |
| | | | EP | 1273273 A2 | 08-01-2003 |
| | | | JP | 2003024343 A | 28-01-2003 |
| | | | US | 2003028193 A1 | 06-02-2003 |
| | | | ZA | 200205288 A | 15-05-2003 |